

## EFFICACY REVIEW

~~Confidential Business Information (CBI) is discussed in this review. Do not disclose CBI to third parties or to anyone lacking appropriate clearances.~~

**Product:** Maki Mini Blocks

**Date:** June 30, 2005

**EPA File Symbol(s):** 7173-202

**DP Bar code(s):** D313869

**Chemical Code:** 112001 Bromadiolone

**Formulation(s):** Bromadiolone bait blocks

**Purpose for Review:** The purpose for this review is to determine if the two submitted studies support the revised basic, 3 alternate CSF's, and support the addition of sewer and burrow use directions on the product label.

**MRID(s):** 464545-01 Hanson, J. M.. September 28, 2004. Bromadiolone Block 9001 (Weathered): Standard Rat Block/Pellet Laboratory Test 1.213 (12/2/90). LiphaTech, Inc. Unpublished Report. Study No. 04062. 65p.

464545-02 Hanson, J. M.. December 22, 2004. Bromadiolone Block 9001 (Weathered): Standard Mouse Block/Pellet Laboratory Test 1.214 (12/2/90). LiphaTech, Inc. Unpublished Report. Study No. 04089. 57p.

**Good Laboratory Practices:** Yes

**Branch Supervisor:** Meredith Laws, Branch Chief

**Team Reviewer:** John Hebert, Product Manager PM Team 07

**IRB Reviewer:** Geraldine R. McCann, Biologist

**BACKGROUND:** LiphaTech, Inc. has applied to amend the current CSF's for the Maki Mini Blocks. The efficacy tests associated with these products were conducted according to the 40 CFR 158.640, Product Performance guidelines 96-10: Commensal Rodenticides: OPP Designation 1.213: Standard Norway Rat Anticoagulant Wax Block and Wax Pellet Laboratory Test Method and OPP Designation 1.214: Standard House Mouse Anticoagulant Wax Block and Wax Pellet Laboratory Test Method. This is a review of the efficacy tests submitted in support of the above named product.

## REVIEW OF DATA:

1. **464545-01** Hanson, J. M.. September 28, 2004. Bromadiolone Block 9001 (Weathered): Standard Rat Block/Pellet Laboratory Test 1.213 (12/2/90). LiphaTech, Inc. Unpublished Report. Study No. 04062. 65p.

**DISCUSSION:** This study was conducted to determine the efficacy of a weathered bait block (Bromadiolone Block 9001) formulated to control male and female Norway rats using a 15-Day, two-choice feeding test (OPP guideline 1.213 Standard Norway Rat Anticoagulant Wax Block and Wax Pellet Laboratory Test Method). Certificates of Analysis were offered for the Bromadiolone bait (Blonde Block 9001) as Lot Number 22304 (manufactured on 08/10/2004) analyzed on 08/17/2004, at 50.37 mg/kg. The bait (BDN Block 9001 [Weathered]) (manufactured on 08/10/2004) was analyzed on 10/06/2004, resulting in 51.21 mg/kg. It is not defined if both baits are the same and analyzed before and after weathering or if these are two different baits.

Forty Wistar-Hannover rats arrived at the test facility at an undetermined date and were weighed on September 07, 2004. The source of the animals is listed as A08/24/04 CRL" (Charles River Laboratories). The testing began September 8<sup>th</sup>, 2004. The OPP guideline 1.213 was used as a protocol reference. The overall difference between the original average pretest weights for the male and female rats used in the test (for both groups, test and control) was 44.14 g. The maximum acceptable difference in average weights between sexes for laboratory rats is 50 g (1.213, 2.1).

The rats were placed in individual, all-metal, mesh-bottom cages. Glass jar feeders were used to issue the bait and diet. AAt least 40 grams of Bromadiolone Block 9001 (weathered )" was available to the animals through day 15 of the test and Athe position of the jars in the cage was reversed on a daily basis.@ "The test substance was presented in the form in which it was manufactured for use and the form in which it was weathered." (ie: presented as whole weathered bait blocks and not altered or cut, shaven, or broken by the personnel).

The raw data to verify the temperature and humidity requirements for weathering the baits was included on page 59 of 65. The temperature of the weathering chamber ranged from 37.7°C to 38°C and the humidity ranged from 92% to 95% during the 15 day process. The raw data to verify temperature and humidity in the testing facility was included with this submission on pages 54 to 58 of 65. The temperature ranged from 67.1°F to 74.3°F and humidity ranged from 47.3% to 69.8%. The records were dated from August 30, 2004 to September 28, 2004 and entered every 2 hours. The guidelines state (1.213, 5.1) the temperature must be kept between 20 to 25°C (68 to 77°F) and humidity between 50 to 55%. One protocol deviation was mentioned on page 44 of 65: "On page 3 of the protocol the temperature is stated to be 68 to 77°F and the relative humidity is stated to be

50-55%. The actual temperature range was from 66.2 to 74.3°F and the humidity range was 45.2 to 69.8%.” What was reported is reasonable and should not affect the results of the test.

The guidelines specify the Standard OPP Rat and Mouse challenge diet to be prepared in a certain way. For these tests, the OPP diet has been labeled with A Lot Number 19104A, 19104B, 21804, and 22404A". Manufactured July 9, 2004, July 9, 2004, August 5, 2004, and August 11, 2004, with corresponding dates of analysis as follows: July 14, 2004, July 14, 2004, August 10, 2004, and August 13, 2004, respectfully.

As stated in the study report: “Each day the unconsumed test substance and challenge diet were collected from the cage and weighed. The quantity of each that was not consumed by the rats during the preceding 24 h was recorded and the amount consumed was calculated. Spilled test substance and challenge diet were recovered and weighed to establish exact consumption data. Where the spillage was damp or fouled by urine or feces, it was dried to approximately its original moisture content before weighing and then thrown out and replaced by fresh product. After the collection and weighing of unconsumed test substance and challenge diet the feed containers were replenished with fresh material. Unconsumed material was reused if it was still in its original form, still retained 50% of its original size, and was not fouled by urine or feces. The test substance was not manipulated in any way (ie: not cut, shaved or broken) when replenishing the food containers.” **The weight of the spillage is not recorded in the raw data presented in the report. No raw data was included with this submission to show how the spillage was incorporated into the consumption equation.**

Of the tested females, only 1 gained weight (10.0 g). All the 19 other tested rats lost weight (0.9 g to 46.1 g). The control males all gained weight (10.6 g to 40.6 g) and of the control females, only 1 lost weight (4.6 g). Overall mortality of the test animals was 100 %. Results of the rat test are summarized below:

**Table 1. Rats on Bromadiolone Bait Blocks (weathered)**  
**Pretest Weights                      Bait 15-Day Test-Consumption and Mortality**

<b>Sex</b>	<b>Average Group Weight (g)</b>	<b>OPP Diet Consumed (g)</b>	<b>Treated Bait Consumed (g)</b>	<b>Total Bait Consumption (g)</b>
M (10)	243.67	1844.5	676.2	2520.7
F (10)	194.44	<b>100% Mortality</b>		<b>Percent Treated Bait Consumed 27.0 %</b>

Total (20)	49.23	Days to death: 4-10 for males and 6-16 for females	
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2. **464545-02** Hanson, J. M.. December 22, 2004. Bromadiolone Block 9001 (Weathered): Standard Mouse Block/Pellet Laboratory Test 1.214 (12/2/90). LiphaTech, Inc. Unpublished Report. Study No. 04089. 57p.

**DISCUSSION:** This study was conducted to determine the efficacy of a weathered bait block (Bromadiolone Block 9001) formulated to control male and female Swiss-Webster mice using a 15-Day, two-choice feeding test (OPP guideline 1.214 Standard House Mouse Anticoagulant Wax Block and Wax Pellet Laboratory Test Method.) Certificates of Analysis were offered for the Bromadiolone bait (BDN Block 9001) as Lot Number 30104 manufactured on 10/27/2004) analyzed on 10/28/2004, at 54.29 mg/kg. The bait (BDN Block 9001 [Weathered]) (manufactured on 10/27/2004) was analyzed on 12/30/2004, resulting in 50.87 mg/kg. It is not defined if both baits are the same and analyzed before and after weathering or if these are two different baits.

Forty Swiss-Webster mice arrived at the test facility at an undetermined date and were weighed on 11/30/2004. The source of the animals is listed as Charles River Laboratories, Inc. The testing began December 2, 2004, and the OPP guideline 1.214 was used as a protocol reference. The overall difference between the original average pretest weights for the male and female mice used in the test (for both groups, test and control) was 4.44g. The maximum acceptable difference in average weights between sexes for laboratory mice is 5g (1.214, 2.1).

The mice were placed in single-sex groups of 10, in all-metal, solid-bottom cages with a bottom surface area of 2.16 ft<sup>2</sup>. "Emptied soup cans (4 per cage) were used to provide shelter." "The test substance and challenge diet were placed in four glass jars each and presented alternately on two plastic trays to capture spillage." "In order to provide the daily food requirement of 10 grams per animal per day minimum, a dosage of at least 100 grams of Bromadiolone Block 9001(weathered) per cage per day through day fifteen was selected via free-choice oral feeding. Challenge diet was also given in greater than or equal to the amount of test substance. The test substance and challenge diet were placed in four glass jars each and presented alternately on two plastic trays to capture spillage. Each day, the unconsumed test substance and challenge diet were collected from the cage and weighed. The quantity of each that was not consumed by mice during the preceding 24 h was recorded, and the amount consumed was calculated. Spilled test substance and challenge diet were recovered and weighed to establish exact consumption data." **The weight of the spillage is not recorded in the raw**

**data presented in the report. No raw data was included with this submission to show how the spillage was incorporated into the consumption equation.**

The raw data to verify the temperature and humidity requirements for weathering the baits was included on pages 44 to 48 of 57. The temperature of the weathering chamber ranged from 36.78°C to 37.39°C (98.2°F to 99.3°F) and the humidity ranged from 86.0% to 92.8% during the 15 day process. The raw data to verify temperature and humidity in the testing facility was included with this submission on pages 49 to 54 of 57. The room temperatures recorded for the test room ranged from 64.4°F to 72.5°F and humidity ranged from 30.6% to 64.1%. The records were dated from November 25, 2004, to December 22, 2004, and entered every 2 hours. The guidelines state (1.213, 5.1) the temperature must be kept between 20 to 25°C (68 to 77°F) and humidity between 50 to 55%.

One protocol Amendment was noted (page 32 of 57): “On page 5 of the protocol, Section 11.1 states “The final report will contain but not be limited to a description of apparatus and procedure, tabular presentation summarizing all results, and a copy of the test substance “formulation sheet” (as a confidential appendix).” Section 11.1 should say: “The final report will contain but not be limited to a description of the objective and procedures and a summary of the results. A copy of the test substance “formulation sheet” will be included in the study file.” The justification then is: “This is what is actually contained in the final report and study file and the change does not affect the study in any way.” The deviation was mentioned on page 33 of 57: “On page 3 of the protocol (Section 5.1) it is stated that the temperature will be 20-25°C (68-77°F), and the humidity will be 50-55%. The actual temperature range was from 64.4 to 72.5°F and the humidity range was 26.1-64.1%.” The justification for the deviation is: “The average temperature during the pre-test and test period was 67.9°F, and the average humidity was 50.5%. The low level humidity logged was during the stabilizing period when the pretest conditions had just begun. Other dips and peaks of humidity and temperature are due to the unpredictable winter weather conditions.”

The raw data to verify the correct formulation of the OPP rat and mouse challenge diet was included with this submission and labeled with Lot numbers 22404B and 22404C (pages 55 and 56 of 57). The Certificate of Analysis (pages 13 and 14) confirm the manufacturing date for both batches.

Of the tested females, all 10 lost weight (1.9 g to 4.1 g). Of the tested males, one gained weight (0.3 g). For the control females, 5 gained weight (0.3g to 1.4g) and 5 lost weight (0.1g to 0.5g). The control males all gained weight (0.6g to 6.2g). Overall mortality of the test animals was 100 %. Results of the mouse test are summarized below:

**Table 2. Mice on Bromadiolone Bait Blocks (weathered)**

**Pretest Weights**

**Bait 15-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	24.85	317.1	141.4	458.5
F (10)	20.35	<p align="center"><b>100% Mortality</b></p> <p align="center">Days to death: 4-8 for males and 4-10 for females</p>		<p align="center"><b>Percent Treated Bait Consumed</b></p> <p align="center"><b>31.0%</b></p>
Total (20)	4.5			

**Efficacy Comments**

1. The raw data from the laboratory conditions for pretest, holding and testing conditions in the animal test facility have been provided for verification.
2. The raw data to verify the correct formulation of the OPP rat and mouse challenge diet and bait formulation were provided for verification. No dye testing was mentioned.  
The bait for both rat and mouse tests was formulated with only no dye, which is the Basic CSF.
3. The weight of the spillage is not recorded in the raw data presented in the report. An explanation of spillage collection was offered in the report; however, no raw data was included with this submission to show the actual record of the spillage was incorporated into the consumption equation.

**Conclusion(s)**

The studies reviewed above are acceptable and support the addition of sewer and burrow use directions on the product label.

**CSF Review**

The new Basic CSF is acceptable and Alternate CSF A (1), Alternate CSF's B (2), and C (3) are also acceptable.

Label Review

1. In the sewer application instructions, there is a typographical error in the second sentence after “suspend bait block”. The label is acceptable.
2. In the FIRST AID statement, modify after “Do not give anything by mouth to an unconscious person.” to include:
  - a. If on skin or clothing: Remove contaminated clothing. Rinse skin immediately with plenty of water for 15 to 20 minutes. Call a poison control center or doctor for treatment advice.
  - b. Have this label with you when obtaining treatment advice.  
Add: a poison control center number (Insert a 24-hour contact number). You may also insert the number for the National Pesticide Information Center number: 1-800-858-7378.